INTERNATIONAL PRELIMINARY EXAMINATION REPORT

Form PCT IPEA 409 (Box V) (July 1998)

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International application No

PCT/US01/06274

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO
Inventive Step (IS)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO
Industrial Applicability (IA)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO

2. citations and explanations (Rule 70.7)

Claims 1-50 meet the criteria set out in PCT Article (4), because the plastid vectors and methods of transformation of plastids have industrial applicability

Claims 1-5, 8-9, 11, 13-32, 34, 37-39 and 41-44 lack novelty under PCT Article 33(2) as being anticipated by Mayfield et al (THE SCRIPPS RESEARCH INSTITUTE, WO 98/31823).

Mayfield et al teach plastid transformation vectors comprising a dimeric IgA gene or a recombinant tetanus toxin single chain antibody; both are operably linked to the psbA promoter and 3' UTR region. Mayfield also teach the transformation of these plasmids into plastids of the lower plant Chlamydomonas and the covalent bonding of the antibody chains in these plastids (pg 76, line 19, to pg 78, line 17; pg 79, line 18 to pg 80, line 5). The dimeric IgA gene comprises a light chain, a heavy chain and a J chain, with stop codons between the chains (Fig. 11). One of these components would be "secretory". These plastids have a selectable marker gene (pg 65, lines 19-23).

In a response filed 7 January, 2002, Applicant urges that Mayfield et al failed to include ribosome binding sites between cistrons and that without these ribosome binding sites, all of the open reading frames in the constructs would not be translated. Applicant also urges that Mayfield et al do not teach that disulfide bonds formed between immunoglobulin chains.

This is not found persuasive. The 5' untranslated region of the chloroplast psbA gene used in the constructs inherently has a ribosome binding site. Additonally, Mayfield et al teach that mutliple proteins are sucessfully expressed from the constructs (pg 78-79). Any immunoglobulin chain produced by the constructs of Mayfield et al would inherently produce disulfide bonds with appropriate other immunoglobulin chains.

Claims 1-5, 37-39 and 50 lack novelty under PCT Article 33(2) as being anticipated by McBride et al (CALGENE LLC, WO 00/03012).

McBride et al teach plant plastid transformation vectors encoding a single chain antibody (claims 11 and 21).

(Continued on Supplemental Sheet.)

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

CLASSIFICATION:

The International Patent Classification (IPC) and/or the National classification are as listed below:
IPC(7): C12N 15/84, 5/04, 15/10, 15/13; A01H 5/10, 5/00; C12P 21/08 and US Cl.: 435/ 320.1, 470, 414, 419, 418, 69.7; 800/288, 293, 317.3, 300; 536/23.4, 23.53

I. BASIS OF REPORT:

This report has been drawn on the basis of the description,
page(s) 1-35, as originally filed.
page(s) NONE, filed with the demand.
and additional amendments:
NONE

This report has been drawn on the basis of the claims,
page(s) NONE, as originally filed.
page(s) NONE, as amended under Article 19.
page(s) NONE, filed with the demand.
and additional amendments:
Pages 36-40 filed with the letter of 7 January, 2002

This report has been drawn on the basis of the drawings,
page(s) 1-8, as originally filed.
page(s) NONE, filed with the demand.
and additional amendments:
NONE

This report has been drawn on the basis of the sequence listing part of the description:
page(s) NONE, as originally filed.
pages(s) NONE, filed with the demand.
and additional amendments:
NONE

V. 1. REASONED STATEMENTS:
The report as to Novelty was positive (YES) with respect to claims 6-7, 10, 12, 33, 35-36, 40, 45-49.
The report as to Novelty was negative (NO) with respect to claims 1-5, 8-9, 11, 13-32, 34, 37-39, 41-44, 50.
The report as to Inventive Step was positive (YES) with respect to claims NONE.
The report as to Inventive Step was negative (NO) with respect to claims 1-50.
The report as to Industrial Applicability was positive (YES) with respect to claims 1-50.
The report as to Industrial Applicability was negative (NO) with respect to claims NONE.

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):

Claims 1-5, 8-9, 11, 13-32, 34-39, 41-44 and 47-50 lack an inventive step under PCT Article 33(3) as being obvious over Mayfield et al (THE SCRIPPS RESEARCH INSTITUTE, WO 98/31823) in view of McBride et al (CALGENE LLC, WO 00/03012).

Mayfield et al teach the production of antibodies in plastids, as discussed above. Mayfield et al do not teach plastid transformation of higher plants.

McBride et al teach higher plant plastid transformation and a variety of plant plastid transformation vectors, including one encoding a single chain antibody (pg 23, lines 1-25; pg 24, line 26, to pg 26, line 16; claims 11 and 21). McBride et al also teach that human proteins expressed in chloroplasts form proper disulfide bonds (pg 41, lines 21-31).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to produce antibodies in

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

plastids as taught by Mayfield et al, and to modify that to express them in plant plastids as described in McBride et al. One of ordinary skill in the art would have been motivated to do so because of the suggestion of Mayfield et al to express their constructs in plants (pg 46-47). Antibodies produced in chloroplasts would not be glycosylated, even though they would contain glycosylation signals, and they would be properly linked through disulfide bridges.

Claims 1-6, 8-9, 11, 13-39, 41-45 and 47-50 lack an inventive step under PCT Article 33(3) as being obvious over the prior art as applied in the immediately preceding paragraph and further in view of Stroger et al (JOHN INNES CENTRE, WO 99/66026).

Mayfield et al in view of McBride et al teach the production of antibodies in plant plastids, as discussed above, but do not teach the production of a greater variety of kinds of antibodies.

Stroger et al the teach expression of antibodies in plants. These antibodies include single chain variable fragments, fragments that comprise the J chain, full-size antibodies, and secretory antibodies (pg 11, line 26, to pg 13, line 13; pg 23, lines 2-10; pg 27, lines 2-7; pg 28, lines 7-13; pg 31, lines 2-21).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to produce antibodies in plant plastids as taught by Mayfield et al in view of McBride et al, and to modify that to express an even greater variety of antibody constructs as described in Stroger et al. One of ordinary skill in the art would have been motivated to do so because of the suggestion of Stroger et al to produce antibodies in chloroplasts (pg 8, lines 5-12).

Claims 1-50 lack an inventive step under PCT Article 33(3) as being obvious over the prior art as applied in the immediately preceding paragraph and further in view of Maliga et al (1999, US Patent 5,877,402).

Mayfield et al in view of McBride et al, further in view of Stroger et al teach the production of a variety of types of antibody constructs in plant plastids, as discussed above. They do not teach constructs with the 16S rRNA promoter, the aadA specitinomycin resistance gene, the psbA 3'region or the 5' part of the trnA gene, nor do they teach contructs where the open reading frames are separated by ribosome binding sites and stop codons.

Maliga et al teach a number of different plastid transformation constructs, including those with the 16S rRNA promoter, the aadA spectinomycin resistance gene, and the psbA 3' region (Fig 22). Maliga et al also teach constructs where the open reading frame is separated by intervening stop codons and ribosome binding sites (column 63, lines 49-67). Maliga et al also describe a plastid transformation vector with the 5' part of the trnA gene is in the flanking region (column 30, lines 33-49; Fig 2).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to produce a variety of different antibodies in plant plastids, as taught by Mayfield et al in view in McBride et al, further in view of Stroger et al, and to modify that to use different plastid transformation constructs as described in Maliga et al. One of ordinary skill in the art would have been motivated to do so because manipulation of the 5' and 3' regulatory regions would increase efficiency and versatility of foreign gene expression (Maliga et al, column 20, lines 36-44).

---------- NEW CITATIONS ----------

NONE

What is claimed is:

1. A plastid transformation and expression vector which comprises an expression cassette comprising as operably linked components, a 5' part of the plastid DNA sequence inclusive of the spacer sequence, a promoter operative in said plastids, a selectable marker sequence, at least one DNA sequence encoding at least a portion of an immunoglobulin chain, a ribosomal binding site adjacent a start codon for said DNA sequence, a transcription termination region functional in said plastid and the 3' part of the plastid DNA sequence, wherein said DNA sequence encodes a polypeptide which forms disulfide bonds between chains.
2. A plastid transformation and expression vector of claim 1 wherein the immunoglobulin chain comprises a heavy chain.
3. A plastid transformation and expression vector of claim 1 wherein the immunoglobulin chain comprises a light chain.
4. A plastid transformation and expression vector of claim 1 wherein the immunoglobutin chain comprises both a heavy and a light chain.
5. A plastid transformation and expression vector of claim 1 wherein the immunoglobulin chain comprises a single-chain variable fragment (scFv).
6. A plastid transformation and expression vector of claim I wherein the immunoglobulin chain comprises a heavy chain constant region fused to an operative ligand.
7. A plastid transformation and expression vector of claim 4 wherein the heavy and light chains are separated by a linker comprising an intervening stop codon and ribosome binding site.
8. A plastid transformation and expression vector of claim 1 which comprises an expression cassette comprising as operably linked components, a 5' part of the plastid DNA inclusive of the spacer sequence, a promoter operative in said plant cell plastids, a selectable marker sequence, a J chain coding sequence, a transcription termination region functional in said cells and the 3' part of the plastid spacer sequence.
9. A vector of claim 8 which comprises a secretary component with the J chain.
10. A vector of claim 9 in which the secretary component and the J chain are separated by a linker which comprises an intervening stop codon and a ribosome binding site.
11. A vector of claim 4 which comprises further a J chain and a secretary component, thereby producing secretary immunoglobulin A (SigA).
12. A plastid transformation and expression vector of claim 1 wherein a 5' part trnA gene is a plastid flanking sequence, the promoter is a 16S rRNA promoter (Prm) driving the selectable marker gene aadA conferring resistance to spectinomycin, the psbA 3' region is a

transcription termination region functional in said cells, and the trnI gene is the 3' part of the plastid spacer, thereby defining the pLD vector.

13. A composition comprising a polypeptide multimer and plant material, wherein said multimer comprises an immunologically active immunoglobulin molecule produced from a DNA sequence integrated into the genome of a plant plastid.
14. The composition of claim 13 wherein said immunoglobulin molecule is nonglycosylated.
15. The composition of claim 13 wherein the DNA sequence encoding said immunoglobulin molecule comprises at least one sequence encoding a glycosylation signal sequence.
16. The composition of claim 14 wherein the DNA sequence encoding said immunoglobulin molecule comprises at least one sequence encoding a glycosylation signal sequence.
17. The composition of claim 13 wherein said immunoglobulin molecule is non-glycosylated.
18. A plant plastid comprising a DNA sequence encoding a polypeptide multimer encoding an immunologically active immunoglobulin molecule.
19. A plant cell comprising at least one plastid of claim 18.
20. A plant comprising at least one plastid of claim 18.
21. A plant plastid preparation comprising plastids of claim 18.
22. A composition comprising a polypeptide multimer and plant material, wherein said multimer comprises an immunologically active non-glycosylated immunoglobulin prepared from plant plastids of claim 18.
23. The composition of claim 13 wherein the polypeptide multimer further comprises a J chain.
24. The composition of claim 13 wherein the polypeptide multimer further comprises a secretary component.
25. The composition of claim 13 wherein the polypeptide multimer further comprises a J chain and secretary component.
26. The composition of claim 17 wherein the polypeptide multimer further comprises secretary component.

27. The composition of claim 17 wherein the polypeptide multimer further comprises a J chain and secretary component.
28. A method for introducing DNA encoding immunoglobulin genes into a plastid, said method comprising: introducing to a plant cell a plastid expression vector adsorbed to a microprojectile, said plastid expression vector comprising as operably linked components, a DNA sequence containing at least one plastid replication origin functional in a plant plastid, a transcriptional initiation region functional in said plant plastid, at least one heterologous DNA sequence encoding at least a portion of an immunoglobulin chain, a ribosomal binding site adjacent a start codon for said DNA sequence, and a transcriptional termination region functional inlaid cells, wherein said DNA sequence encodes a polypeptide which forms disulfide bonds between chains, whereby said heterologous DNA is introduced into plastid in said plant cell.
29. The method of claim 28 wherein the immunoglobulin chain comprises a heavy chain.
30. The method of claim 28 wherein the immunoglobulin chain comprises a light chain.
31. The method of claim 28 wherein the immunoglobulin chain comprises both a heavy chain and a light chain.
32. The method of claim 28 wherein the immunoglobulin chain comprises a singlechain variable fragment (scFv).
33. The method of claim 28 wherein the immunoglobulin chain comprises a heavy chain constant region fused to an operative ligand.
34. The method of claim 28 wherein said plastid expression vector further comprises DNA sequences encoding a J chain.
35. The method of claim 28 wherein said plastid expression vector further comprises DNA sequences encoding a secretary component.
36. The method of claim 28 wherein said plastid expression vector further comprises DNA sequences encoding a J chain and a secretary component, thereby producing secretary immunoglobulin (SigA).
37. A plastid transformation and expression vector which comprises an expression cassette comprising an operably linked components, a promoter operative in plant plastids, a selectable marker sequence, immunoglobulin chain coding sequences, a ribosomal binding site adjacent start codons for said sequences, a transcription termination region functional in said cells.
38. A plastid transformation and expression vector of claim 37 wherein the immunoglobulin chains comprise heavy chains and light chains.

39. A plastid transformation and expression vector of claim 38 which comprises covalent boding between the chains, into immunologically active immunoglobulins in the plastid.
40. A plastid transformation and expression vector of claim 39 wherein the heavy and light chains are separated by a linker comprising an intervening stop codon and ribosome binding site.
41. A plastid transformation and expression vector which comprises an expression cassette comprising an operably linked components, a promoter operative in plant cell plastids, a selectable marker, a J chain coding sequence, a ribosomal binding site adjacent a start codon for said J chain coding sequence, a transcription termination region functional in said cells.
42. A vector of claim 41 which comprises a secretary component with the J chain.
43. A vector of claim 42 which the secretary component and the J chain are separated by a linker which comprises an intervening stop codon and a ribosome binding site.
44. A vector of claim 38 which comprises further a J chain and a secretary component, thereby producing secretary immunoglobulin A (SigA).
45. A plastid transformation and expression vector of claim 44 which comprises in addition that the light chains are four identical light chains, and the heavy chains are four chains.
46. A plastid transformation and expression vector of claim 38 wherein the promoter is a 16S rRNA promoter (Prm) driving the selectable marker gene aadA conferring resistance to spectinomycin, and the psbA 3' region is a transcription region functional in said cells, thereby defining the pZS vector.
47. The stably transformed plant which has been transformed by the vector of claim 37 and the progeny thereof.
48. The progeny of the stably transformed plant of claim 47, wherein such progeny are seeds.
49. The plant of claim 47, wherein the plant is tobacco.
50. A universal plastid transformation and expression vector which comprises an expression cassette comprising as operably linked components, a 5' part of the plastid spacer sequence, a promoter operative in said plant cell plastids, a selectable sequence marker, at least one DNA sequence encoding at least a portion of a immunioglobulin chain, a ribosomal binding site adjacent a start codon for said DNA sequence, a transcription termination region functional in said cells and the 3' part of the plastid spacer and flanking each side of the expression cassette, flanking DNA sequences which are homologous to a DNA sequence inclusive of a spacer sequence conserved in the plastid genome of different plant species, wherein said DNA sequence encodes a polypeptide which forms disulfide bonds between chains, whereby stable integration of the heterologous coding sequence into the plastid genome

of the target plant is facilitated through homologous recombination of the flanking sequences with the homologous sequences in the target plastid genome.

51. The stably transformed plant which has been transformed by the vector of claim 41 and the progeny thereof.

52. The progeny of the stably transformed plant of claim 51, wherein such progeny are seeds.

PCT US01 06274

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 20 November 2001 (20.11.01)	
International application No. PCT/US01/06274	**Applicant's or agent's file reference** 1463-PCT-00
International filing date (day/month/year) 28 February 2001 (28.02.01)	**Priority date** (day/month/year) 29 February 2000 (29.02.00)
Applicant DANIELL, Henry et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

21 September 2001 (21.09.01)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Sean Taylor
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

Copy for the Elected Office (EO/US)

PCT/US01/06274

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

To:

DONATIELLO, Guy, T.
Schnader Harrison Segal & Lewis, LLP
1600 Market Street - Suite 3600
Philadelphia, PA 19103
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year)
20 novembre 2001 (20.11.01)

Applicant's or agent's file reference
1463-PCT-00

IMPORTANT NOTIFICATION

International application No.
PCT/US01/06274

International filing date (day/month/year)
28 février 2001 (28.02.01)

1. The following indications appeared on record concerning:

[ ] the applicant [ ] the inventor [X] the agent [ ] the common representative

Name and Address
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Philadelphia, PA 19103-7286
United States of America

State of Nationality:
State of Residence:
Telephone No.: 215-751-2427
Facsimile No.: 215-568-6946
Teleprinter No.:

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[X] the person [ ] the name [ ] the address [ ] the nationality [ ] the residence

Name and Address
DONATIELLO, Guy, T.
Schnader Harrison Segal & Lewis, LLP
1600 Market Street - Suite 3600
Philadelphia, PA 19103
United States of America

State of Nationality:
State of Residence:
Telephone No.: (215) 751-2463
Facsimile No.: (215) 972-7238
Teleprinter No.:

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

[X] the receiving Office
[ ] the International Searching Authority
[X] the International Preliminary Examining Authority
[ ] the designated Offices concerned
[X] the elected Offices concerned
[ ] other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer
Sean Taylor

Telephone No.: (41-22) 338.83.38

Form PCT/IB/306 (March 1994)

004468607

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/06274

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: **48 and 49**
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/06274

A. CLASSIFICATION OF SUBJECT MATTER:
US CL :

435/ 320.1, 470, 414, 419, 418, 69.7; 800/288, 293, 317.3, 300; 536/23.4, 23.53

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/06274

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :C12N 15/84, 5/04, 15/10, 15/13; A01H 5/10, 5/00; C12P 21/08

US CL :Please See Extra Sheet.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/ 320.1, 470, 414, 419, 418, 69.7; 800/288, 293, 317.3, 300; 536/23.4, 23.53

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

AGRICOLA, BIOSIS, CABA, CAPLUS, USPAT, JPO, EPO, DERWENT
search terms: (plastid or chloroplast) transformation; (antibod? or immunoglob?);

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,451,513 A (MALIGA et al) 19 September 1995, col. 9, lines 24-34 and col. 13, line 66, to col. 14, line 20.	1-11, 13-48, 50
Y	WO 99/66026 A2 (STROGER et al) 23 December 1999, page 8, lines 5-12, page 11, line 26 to page 13, line 13, page 23, lines 2-10, page 27, lines 2-7, page 28, lines 7-13, page 31, lines 2-21.	1-48, 50
X	WO 00/03012 A2 (MCBRIDE et al) 20 January 2000, page 18, lines 12-22, page 23, lines 2-25, page 42, lines 16-28, claims 11 and 21.	1-5, 13, 18-21, 28-32, 37-39, 50
Y		6-12, 14-17, 22-27, 33-36, 40-48

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 26 APRIL 2001	Date of mailing of the international search report 06 JUN 2001
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer ANNE R. KUBELIK Telephone No. (703) 308-0196

Form PCT/ISA/210 (second sheet) (July 1998) *

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/06274

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,877,402 A (MALIGA et al) 02 March 1999, Figure 22C, col. 34, line 54, to col. 38, line 24.	1-11, 13-47, 50
X	WO 98/31823 A1 (MAYFIELD, S.) 23 July 1998, page 76, line 19, to page 78, line 17, and page 79, line 18, to page 80, line 25.	1-5, 8-11, 28-32, 34-39, 41-44
Y		6-7, 33, 40, 45